



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/785,230	02/25/2004	Tadamitsu Kishimoto	046124-5042-01	1453

9629 7590 01/08/2009
MORGAN LEWIS & BOCKIUS LLP
1111 PENNSYLVANIA AVENUE NW
WASHINGTON, DC 20004

EXAMINER

GODDARD, LAURA B

ART UNIT	PAPER NUMBER
----------	--------------

1642

MAIL DATE	DELIVERY MODE
-----------	---------------

01/08/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/785,230	Applicant(s) KISHIMOTO ET AL.	
	Examiner LAURA B. GODDARD	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 October 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 25, 26 and 28 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 25, 26 and 28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☒ Certified copies of the priority documents have been received in Application No. 09/646,785.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>12/5/08</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The Amendment filed October 22, 2008 and IDS filed December 5, 2008 in response to the Office Action of October 2, 2008, are acknowledged and have been entered. Claims 1-23, 27, 29, and 30 were canceled and claims 25, 26, and 28 were amended in the Examiner's Amendment mailed October 2, 2008. Claims 25, 26, and 28 are currently pending and being examined.

New Rejection

(based on new considerations)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 25, 26, and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Arenberg et al (J Clinical Investigation, 1996, 97:2792-2802) and Strieter et al (J of Leukocyte Biology, 1995, 57: 752-762, IDS), in view of Rafii et al (An AACR Special Conference in Cancer Research, Proceedings, January 1998, p. 1-2, IDS), Gupta et al (J Biological Chemistry, February 1998, 273: 4282-4287, IDS), Volin et al (Biochemical and Biophysical Research Communications, January 1998, 242:46-53, IDS), and Doranz et al (J Exp Med, October 1997, 186:1395-1400, IDS).

The claims are drawn to a method for treating a solid tumor comprising administering a substance that inhibits human CXCR4 to a human subject expressing CXCR4 in need thereof, wherein the substance inhibits binding between the human ligand SDF-1 and the human receptor CXCR4, wherein the substance is selected from the group consisting of: i) an anti-human CXCR4 antibody or ii) an anti-human SDF-1 antibody (claim 25), a method for treating a disease pathologically caused by neovascularization comprising administering a substance that inhibits human CXCR4 to a human subject expressing CXCR4 in need thereof, wherein the substance inhibits binding between the human ligand SDF-1 and the human receptor CXCR4, wherein the substance is selected from the group consisting of: i) an anti-human CXCR4 antibody or ii) an anti-human SDF-1 antibody (claim 26), a method for suppressing vascularization comprising administering a substance that inhibits human CXCR4 to a human subject expressing CXCR4 in need thereof, wherein the substance inhibits binding between the human ligand SDF-1 and the human receptor CXCR4, wherein the substance is selected from the group consisting of: i) an anti-human CXCR4 antibody or ii) an anti-human SDF-1 antibody (claim 28).

Arenberg et al teach a method of treating human non-small cell lung cancer (NSCLC) xenografts (which is a solid tumor and disease pathologically caused by neovascularization) in mice comprising administering a neutralizing antibody to CXC chemokine IL-8 (abstract; p. 2792, col. 2; Figure 5). Arenberg et al teach that the antibodies decreased angiogenic activity and reduced tumor vessel density (suppressed vascularization) (Figure 7; p. 2796, col. 1-2; Table III) and members of the CXC

Art Unit: 1642

chemokine family can function as angiogenic or angiostatic factors in regulating neovascularization (p. 2800, col. 2).

Strieter et al also teach angiogenesis associated with NSCLC tumor growth is dependent on members of the CXC chemokine family acting either as angiogenic or angiostatic factors. This paradigm predicts that a shift in the balance of expression of these CXC chemokines dictates whether the neoplasm grows and develops metastatic potential or regresses. The net angiogenic activity during the progression of tumorigenesis is mediated by the biological imbalance that favors the expression of angiogenic CXC chemokines compared with the angiostatic chemokines (p. 755, col. 2 bridging to p. 756, col. 1; p. 759, col. 1, last paragraph). Strieter et al teach that CXC chemokines are likely candidates to target specific therapies for attenuating tumor growth and metastasis (abstract; p. 756, col. 2, top).

Arenberg et al and Strieter et al do not teach treating humans expressing CXCR4 or administering an anti-human CXCR4 antibody or an anti-human SDF-1 antibody that inhibits the binding between SDF-1 and CXCR4.

Rafii et al teach that bone marrow derived hematopoietic stem cells (which mature to endothelial cells) express CXCR4, the receptor for chemokine SDF-1, and that incubation of the stem cells in the presence of SDF-1 induced the cells to migrate. Rafii et al teach that SDF-1 chemokine recruits the cells to peripheral circulation and can play a role in the acceleration of vascular endothelialization process (abstract, p. 2).

Gupta et al teach that chemokine SDF-1 induced human endothelial cells to migrate (p. 4268, both columns). Gupta et al teach that chemokines and their receptors,

Art Unit: 1642

especially SDF-1 and CXCR4, may play a role in the etiology of the endothelial cell response during vascular disease and inflammation (p. 4287, col. 1). Gupta et al suggest using CXCR4 antibodies and antagonists to study the role of CXCR4 (p. 4287, col 1).

Volin et al also teach that CXCR4 and SDF-1 play a role in vascular homeostasis and pathophysiology (abstract). Volin et al teach that blood vessel endothelial cells express chemokine receptor CXCR4 using monoclonal antibody 12G5 that binds CXCR4 (p. 48; Figure 5). Volin et al teach CXCR4's ligand SDF-1 is a chemoattractant for lymphocytes and monocytes (p. 50).

Doranz et al teach that monoclonal antibody 12G5 binds CXCR4 at the SDF-1 activation site and inhibits SDF-1 signaling (p. 1397, col. 2, bottom; p. 1398, col. 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to treat a solid tumor, disease pathologically caused by neovascularization, or suppress vascularization in humans expressing CXCR4 in the methods of Arenberg et al or Strieter et al comprising administering a neutralizing antibody to chemokine receptor CXCR4 or chemokine SDF-1 because both references teach that chemokines play a role in angiogenesis and tumor growth and these can be inhibited by a neutralizing antibody. One would have been motivated to administer a neutralizing antibody to human chemokine receptor CXCR4 or chemokine SDF-1 in the method of Arenberg et al or Strieter et al because CXCR4 and SDF-1 are known contributors to endothelial cell migration and vascularization (as taught by Rafii et al, Gupta et al, Volin et al) and vascularization is a known contributor to tumor growth

Art Unit: 1642

(Arenberg et al and Strieter et al). One of ordinary skill in the art would have a reasonable expectation of success treating a solid tumor, disease pathologically caused by neovascularization, or suppressing vascularization in humans expressing CXCR4 because neutralizing antibodies blocking CXCR4 and SDF-1 signaling are known (as taught by Doranz) and because Arenberg et al demonstrate the successful inhibition of human tumor growth and vascularization *in vivo* by administering chemokine neutralizing antibodies.

3. All other objections recited in the Office Action mailed October 2, 2008 are hereby withdrawn in view of corrections to the sequence listing.

4. **Conclusion:** No claim is allowed.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAURA B. GODDARD whose telephone number is (571)272-8788. The examiner can normally be reached on 7:00am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1642

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Laura B Goddard/
Examiner, Art Unit 1642